# PARADIGM BIOPHARMA

BELL POTTER HEALTHCARE CONFERENCE

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# Executive Summary

## Lead program:

Phase 3 global study in Knee OA. Blockbuster potential with 32m+ sufferers in the US alone

Proven Safety and Efficacy: OA Phase 2b trial (n=112) met primary, secondary and exploratory endpoints: Included pain, function, BML and biomarkers

## Commercial:

Global Market Research confirmed US$2500 achievable for Zilosul® for indication of pain and function in knee OA.

## Pipeline:

Multiple indications in various stages of development:

Clinical Stages: OA, MPS, Alphavirus

Pre-Clinical: Respiratory, Heart Failure.

## Protection:

Strong portfolio of IP protection and patents on Zilosul® – patents in all key markets from 2030 to 2039.

Exclusive agreement with only FDA approved manufacturer of PPS, bene pharmaChem, for 25 years from date of marketing approval.

Exclusive agreement covers all major markets.

# Phase 3 Company

## Global Harmonised Pivotal Trial – PARA_OA_002

### United States

- FDA clears IND application investigating Pentosan Polysulphate Sodium (PPS) for the treatment of pain associated with knee osteoarthritis (the Trial) has been cleared by the US FDA
- Approximately 56 sites have been selected.
- Lead investigator confirmed.
- Central Ethics approval received.

### Australia

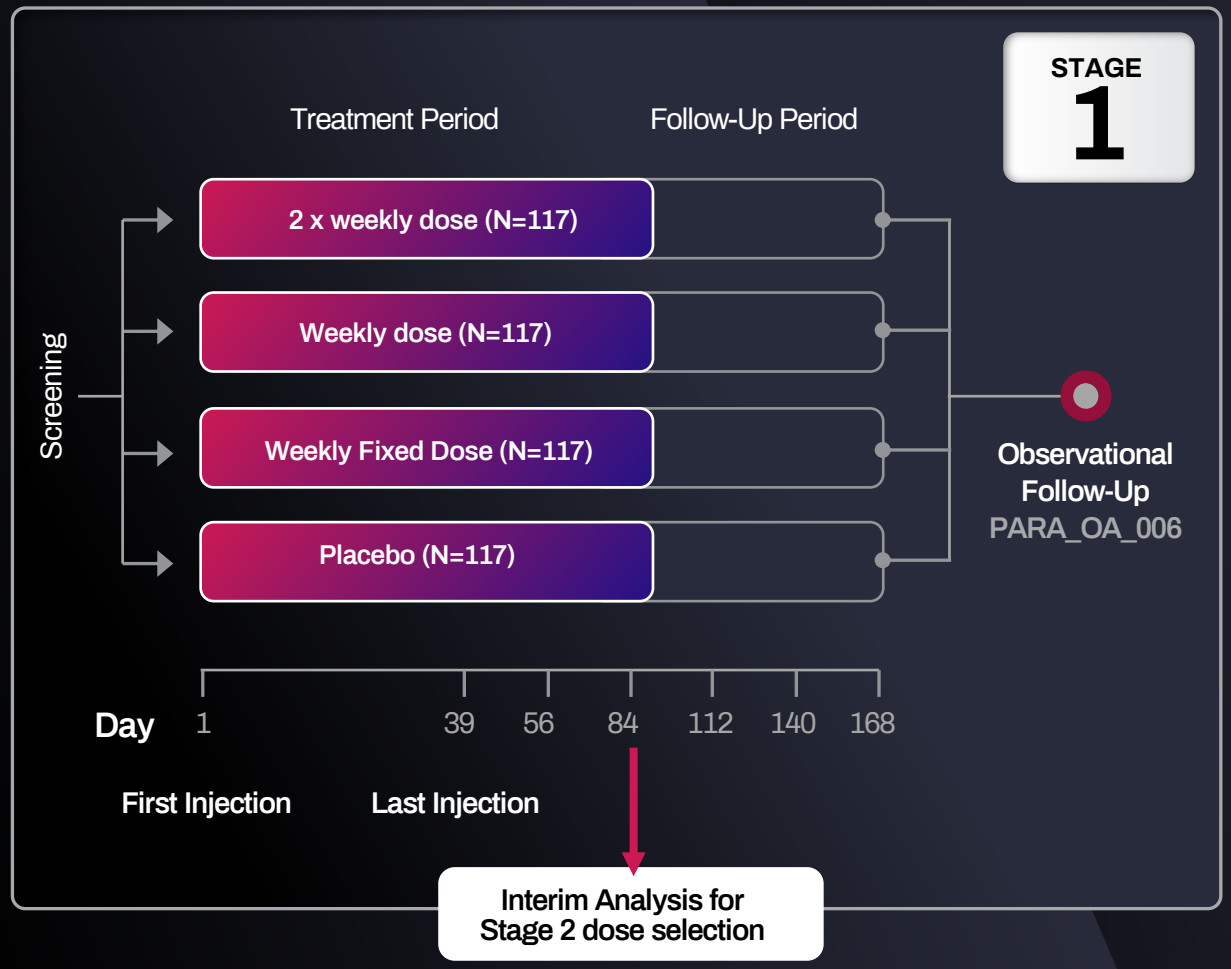
- Eight (8) sites have been selected.
- Protocol has received ethics approval.
- Paradigm has begun contracting sites in WA, Victoria, NSW, SA and QLD.
- First 4 sites in Australia have initiated screening participants
- Lead investigator confirmed.

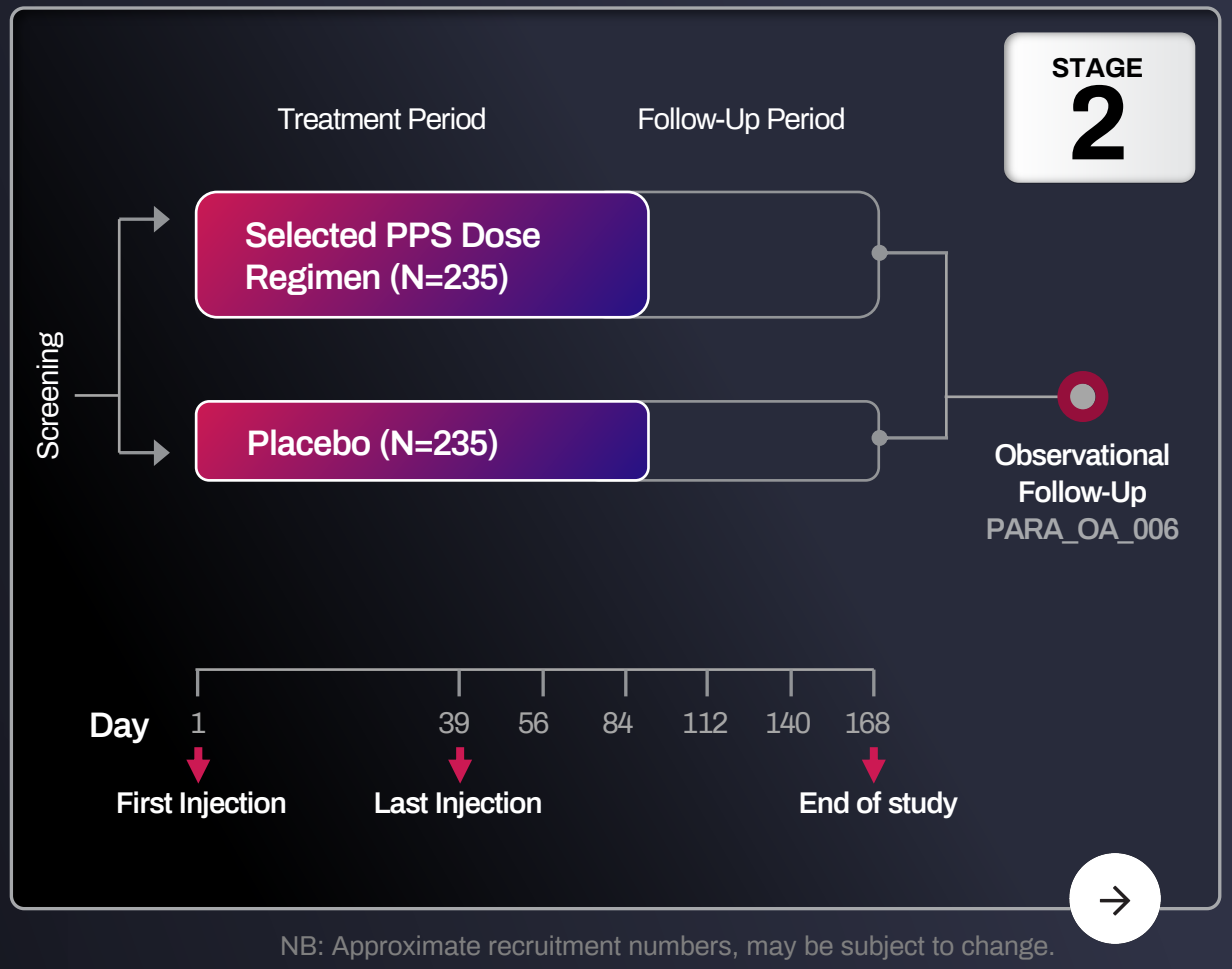
### Europe and UK

- Twelve (12) sites to be initiated
- Paradigm is finalising discussion with the lead investigator.
- Site initiation and screening to commence in CY2022

# Phase 3 Trial Design

## Trial Design




NB: Approximate recruitment numbers, may be subject to change.

# Blockbuster market opportunity

## Zilosul® aims to meet a significant unmet need in osteoarthritis

Total prevalence of OA in key markets

**72M+**

and growing

USA | CAN | EU5 | AUS

OA in the US alone is predicted to increase by 86% to 67 million by 2030.[3]

Knee and Hip

**69%**

OA patients dissatisfied with current treatments[1]

**81%**

Target uptake: 10% dissatisfied market[1]

Zilosul® indicative price: US$2500 per year[2]

1. National Institute of Health; Emerging drugs for osteoarthritis; Hunter DJ and Matthews G 16(3): 479–491; 2011 September.
2. Global Pricing Research conducted by Paradigm. EU5: Germany, UK, Spain, France, Italy
3. OARSI. Osteoarthritis: A Serious Disease, Submitted to the U.S. Food and Drug Administration December 1, 2016

# Global Market Research

- In 2021 Paradigm conducted market research in major global markets, with physicians, funding decision makers (payers) and patients to better understand willingness-to-pay and willingness-to-prescribe Zilosul for osteoarthritis of the knee (kOA)
- The research centred around 3 key questions in two scenarios:
  1. Zilosul registered for pain and function (P&F) only
  2. Zilosul registered for pain, function and disease modification (DM).

**1**

**How is Zilosul perceived by physicians & public payers?**

**2**

**How will Zilosul fit in the Tx algorithm & how would physicians use it?**

**3**

**How much would public payers and patients pay for Zilosul?**

# Zilosul's proposed profile was regarded positively

**Assuming sustained efficacy and robust safety data, physicians and payers believe Zilosul® will provide high value to the treatment of kOA by covering some important unmet needs**

New MoA

Favourable safety profile with no renal, GI, CV side effects or cartilage degradation ★

No drug abuse potential ★

**ZILOSUL®**

Meaningful pain reduction, functional improvement and potential DM effect ★

Sub-Cutaneous RoA vs. IA injections

Convenient dosing regimen (1 weekly injection for 6 weeks) vs. daily intake

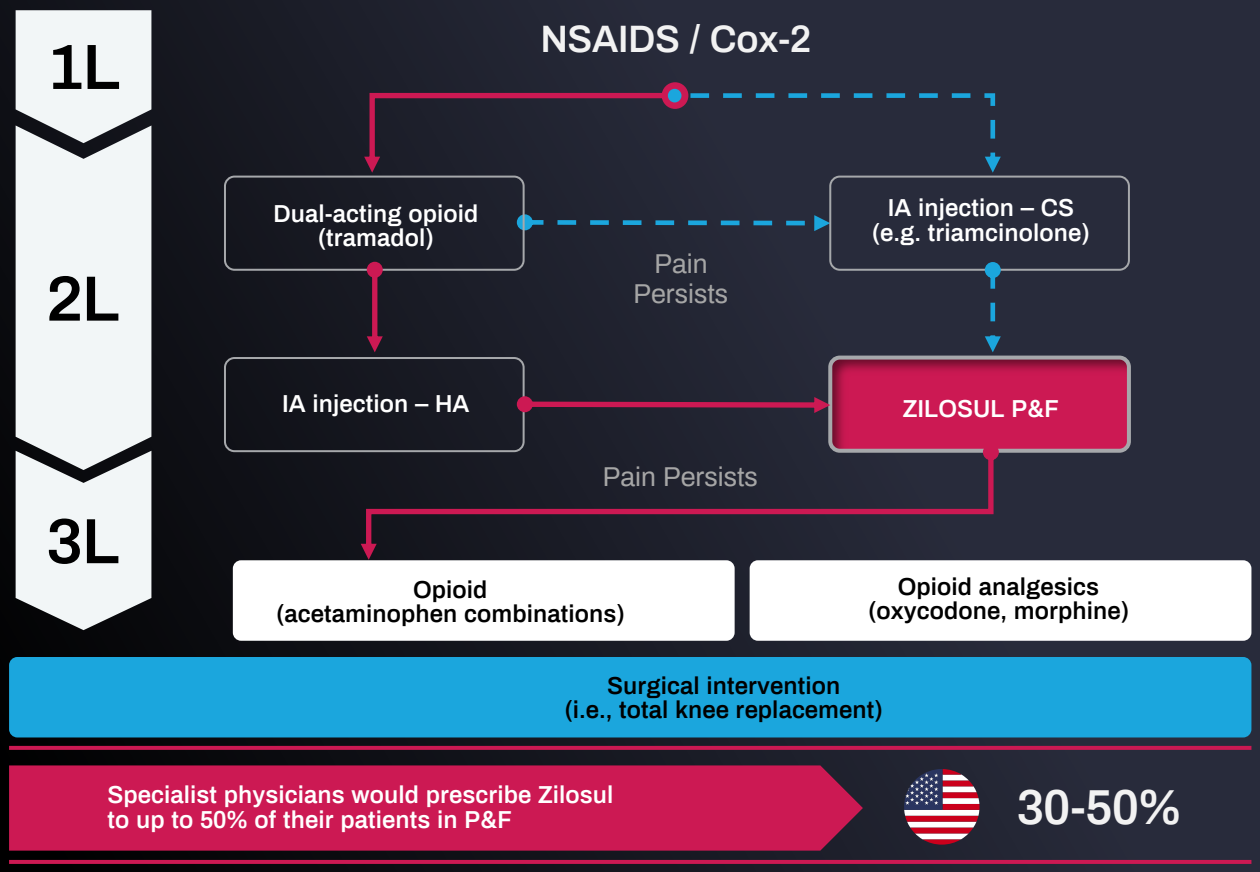
Zilosul is expected to cover the main residual unmet needs highlighted by physicians and payers as it will provide an alternative treatment to kOA patients that is well-tolerated and potentially preserving structural changes in kOA

*CV = Cardiovascular; DM = Disease Modification; GI = Gastrointestinal; IA = Intra-articular; kOA = Knee Osteoarthritis; MoA = Mechanism of Action; RoA = Route of administration*

★ *Zilosul addresses the key residual unmet needs identified by payers and KOLs*

# Pain & function

## Physicians may consider Zilosul® as a second line therapy

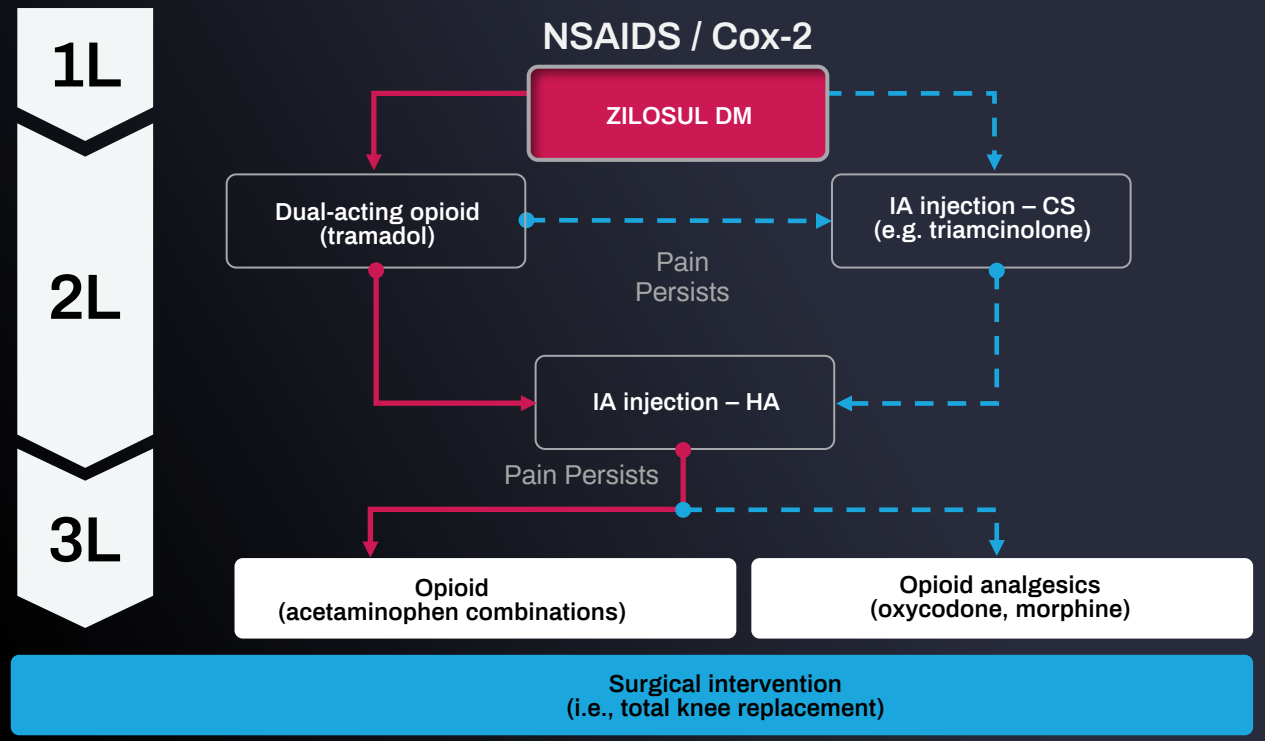



Main Tx
Alternative Tx

*CV = Cardiovascular; DM = Disease Modification; GI = Gastrointestinal; IA = Intra-articular; kOA = Knee Osteoarthritis; MoA = Mechanism of Action; RoA = Route of administration*

# Disease modification

## Zilosul® may be used early in therapy




Main Tx
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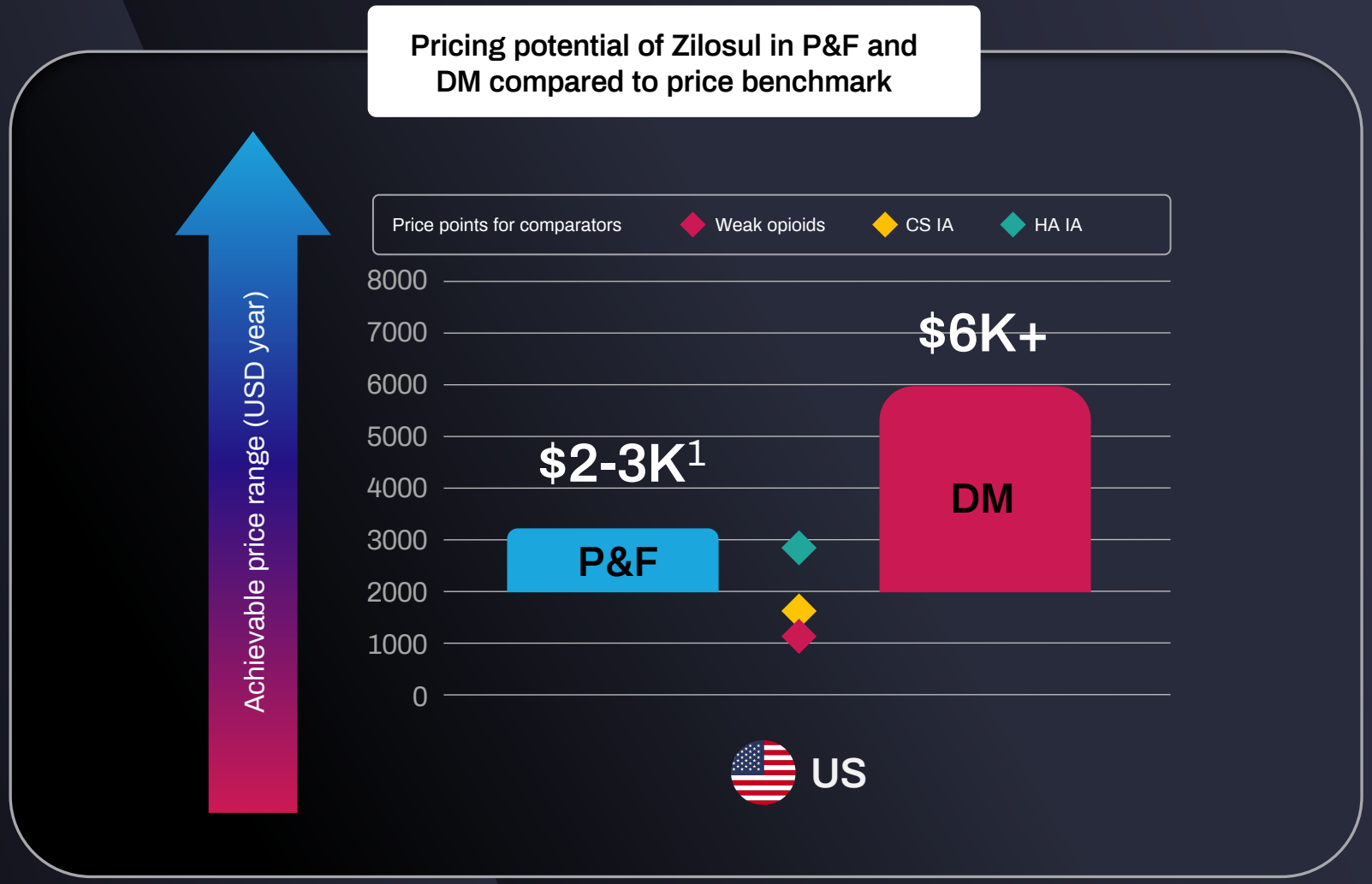
# Target pricing

## Achievable for P&F and a significantly higher price for DM




*1. Reasonable price - higher prices may be achievable but will likely trigger restrictions on use by payers*

# DMOAD

## Current programs to inform of Zilosul® potential as a DMOAD

### PARA_OA_008 - Australia

- Biomarker study assessing change from baseline in multiple objective measures associated with disease progression of OA.
- Study will randomise 60 participants to receive PPS or Placebo.
- To date the exploratory clinical trial is 50% recruited.
- Protocol amendments include once weekly dosing regimen, second trial site initiated, extended follow-up period to 12-months.

### Canine OA Study

- Dogs with OA of the stifle joint are treated with PPS at a dosing of 3mg/kg (1.7mg/kg human equivalent) weekly for 6-weeks.
- Pain and function will be assessed together with structural changes from baseline as determined by the global OA score measured by X-ray and bone marrow lesions and cartilage volume by MRI.
- Serum samples will also be taken to measure biomarker levels associated with inflammation, cartilage degradation and pain.
- The longer follow up period of 20 weeks (equates on average to a period of 3 years in human lifespan)

# MPS

## Clinical programs in Orphan designation Paradigm is enrolling

### MPS I - Australia

- Open label trial currently enrolling up to 10 subjects. Dosed weekly for 12 weeks then every other week for a total of 52 weeks.
- Women's & Children's Hospital Adelaide.
- Primary endpoint is safety, key secondary endpoints are pain and function, as well as PK.
- 3 subjects currently in treatment: enrolment of additional patients ongoing.
- PPS has been well tolerated.
- Presentation at ICIEM – Congress of Inborn Errors of Metabolism. Nov 2021

### MPS VI - Brazil

- A double-blind placebo-controlled trial with 12 subjects. Dosed weekly for 24-weeks.
- Primary endpoint is safety, key secondary endpoints are pain and function.
- The Brazilian regulatory agency, ANVISA, and Brazilian ethics committee CONEP have approved Paradigm's clinical program and study endpoints.
- First patient dosed.

# R&D Pipeline

Repurposing of PPS across several acute and chronic medical indications.

| Indication / Action of PPS | Stage of Development | Status |
|---|---|---|
| **Alphavirus induced arthralgia**<br>• Anti-inflammatory target: NF-kB<br>• Pain target: NGF<br>• Cartilage degeneration target: ADAMTS-5; MMPs | • Preclinical Proof-of concept for CHIK-V: (Institute for Glycomics; Queensland) | Completed |
| **Heart Failure**<br>• Adverse tissue remodeling target: ADAMTS-4<br>• Anti-inflammatory target: NF-kB<br>• Vascular endothelial inflammation target: CAM (Cell Adhesion Molecules) | • Preclinical Dose translational study: (Center for Heart Failure Research & Institute for Experimental Research, Oslo University, Oslo) | Results Pending |
| **Acute Respiratory Distress Syndrome (viral-induced)**<br>• Cytokine storm anti-inflammatory target: NF-kB<br>• Inhibition of Compliment activation | • Preclinical Proof-of-concept study: (Menzies Health Institute, Queensland)<br>  • Top-Line results from preclinical mouse model of ARDS mediated by influenza infection | Ongoing |

For more information please visit:
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